A. Rejection under 35 U.S.C. § 101

The rejection of claims 15, 16, 18 to 22 and 44 under 35 U.S.C. § 101 as allegedly lacking utility respectfully is traversed.

It is maintained in the present Office Action, for the reasons set forth in the previous Office Action (mailed 8/29,2000; paper no. 5), that the specification does not disclose a biological function of GDF-12 and that there is no evidence or record or scientific rationale to support an associate of the claimed invention with a particular liver disorder. As such, it is alleged that the is not specific and substantial credible utility disclosed in the specification nor is there a well established utility.

Applicants submit that a method of detecting a cell proliferative disorder by determining an amount of a protein produced by cells involved in the disorder, including the disclosed method of detecting a liver disorder based on determining the amount of GDF-12, is well established utility. The levels of various proteins, including cyclin D1, PCNA, prothrombin, and others as set forth in the response to the previous Office Action, are known to correlate with the level of proliferation of cells producing these proteins and detection of such proteins has been used in diagnostic procedures. Thus, it is a well known that an amount of a protein produced by particular cells, including the amount of GDF-12 produced by liver cells as disclosed in the subject application, can be directly related to the number of cells producing the protein, and, it is submitted, is a well established utility that a determination of the levels of such proteins can be diagnostic of a particular tissue containing cells that produce the protein. As such, the skilled artisan, viewing the subject application, clearly would have known that an increased proliferation of hepatocytes due, for example, to liver cancer, can result in increased GDF-12 levels as detected using an anti-GDF-12 antibody (see page 6, lines 11-16), whereas a liver disease such as cirrhosis, which is associated with decreased numbers of viable hepatocytes, can be identified by detecting a relatively decreased amount of GDF-12.

In the previous Action, it was alleged, in part, that the use of an antibody to GDF-12 as a diagnostic is clearly to use it as the object of further research. Applicants respectfully disagree, however, and point out that the mere fact that the biological function of a protein may not be completely defined does not impact the utility of the protein as a diagnostic marker. For example, the level of prostate-specific antigen (PSA) in the blood is well recognized as a diagnostic marker of prostate disease, even though the function of PSA was not known. Thus, even where the function of a protein such as PSA was not known, it was recognized that the level of PSA was increased above normal in benign prostate hyperplasia and in prostate carcinoma, presumably due, at least in part, to the increased number of prostate cells associated with these conditions. As such, it is submitted that there is no requirement that a biological function of a protein be known in order to provide a patentable utility because the biological function of GDF-12 is not relevant to the claimed methods.

It is further submitted that an anti-GDF-12 antibody as disclosed in the subject application is useful as a research tool, including as a diagnostic reagent. Applicants point out that a research tool clearly is a patentable utility, and is readily distinguishable from an "object of further research" as stated in the previous Office Action. In the present case, an anti-GDF-12 antibody is useful *per se* to detect GDF-12 levels in a specimen from a subject, including from a liver specimen, wherein the level of GDF-12 is indicative of a liver disorder.

In summary, it is submitted that the use of an antibody to determine the level of a protein, wherein the level of the protein is diagnostic of the proliferative state of cells that produce the protein, is a well established utility, and that, in view of the subject application, one skilled in the art clearly would have recognized that an anti-GDF-12 antibody can be used to determine levels of GDF-12, which can be indicative of a liver disorder.. Accordingly, it is respectfully requested that the rejection of the claims under 35 U.S.C. § 101 be removed.

C. Rejections under 35 U.S.C. § 112

The objection to the specification and corresponding rejection of claims 15, 16, 18 to 22 and 44 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement respectfully are traversed.

For the reasons set forth above, it is submitted that the specification discloses a patentable utility, and it is further submitted that the specification teaches how to make and use an anti-GDF-12 antibody for purposes of practicing the claimed methods (pages 13, line 23, to page 16, line 2). As such, it is respectfully requested that this objection to the specification be withdrawn and that the corresponding rejection of the claims under 35 U.S.C. § 112, first paragraph, be removed.

In view of the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect respectfully is requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: July 20, 2001

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